

Supplemental Table 1. IH specimen/cell demographics and β AR expression

Specimen	Sex	Age	Ethnicity	Location	Phase	β 1AR	β 2AR
Hem41	Male	6 mos	½ White, ½ Asian	Forehead	Proliferating	+/-	+++
Hem49	Female	1.5 yrs	White	Cheek	Involuting (w/ Pockets of Proliferating)	+/-	++
Hem50	Male	2 yrs	White	Forehead	Proliferating	+/-	++

+/- low levels/undetectable, ++ moderate levels, +++ high levels

Supplemental Figures

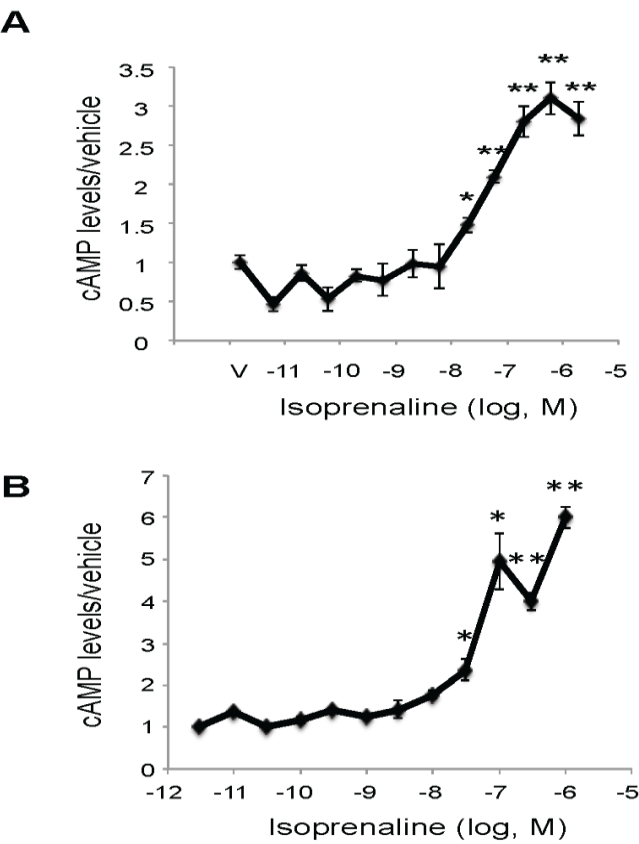
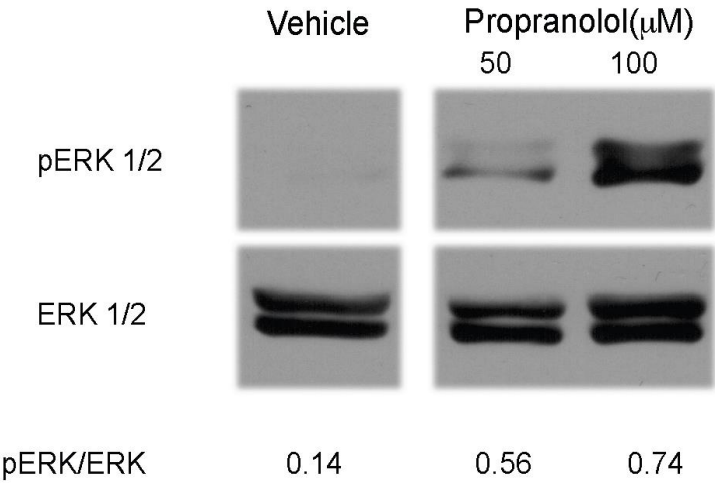


Figure S1. In HemSCs, β AR agonist upregulated cAMP levels via $G_{\alpha s}$. **A)** HemSCs were treated with increasing doses of isoprenaline over a 7-log dose range (10^{-11} M to 10^{-5} M) and cAMP levels determined. **B)** HemSCs were treated with increasing doses of isoprenaline over a 7-log dose range (10^{-11} M to 10^{-5} M) in the presence of 10 μ M forskolin. An increase in cAMP levels indicates that β AR signaling activates the $G_{\alpha s}$ pathway in HemSCs, as signaling via a $G_{\alpha i}$ pathway would decrease cAMP levels in the presence of forskolin. **A,B)** Data represented as cAMP levels relative to vehicle (V) \pm S.E.M. * $p < 0.05$, ** $p < 0.005$.

A



B

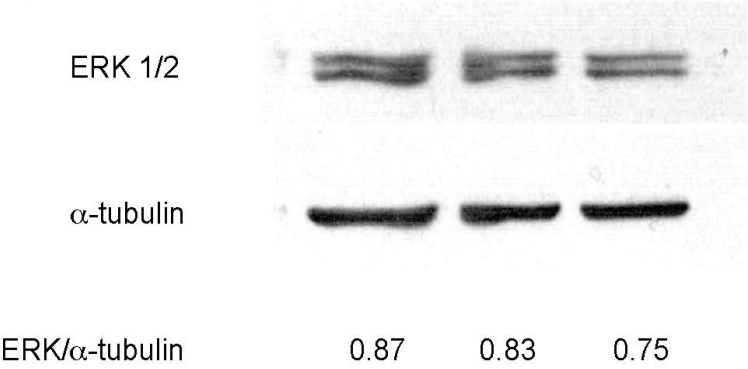


Figure S2. Propranolol activated ERK1/2 in bone marrow-derived mesenchymal stem cells (MSCs).

MSCs were treated with vehicle or 50 μ M and 100 μ M propranolol and ERK1/2 activation determined at 30 minutes. **A)** Total and phospho-ERK1/2 (p-ERK1/2) expression was assessed by Western blot. Ratio of p-ERK1/2:ERK1/2 as determined by densitometry presented below blots. **B)** Total ERK1/2 and α -tubulin (protein loading control) expression was assessed by Western blot. Ratio of total ERK1/2: α -tubulin presented below blots.

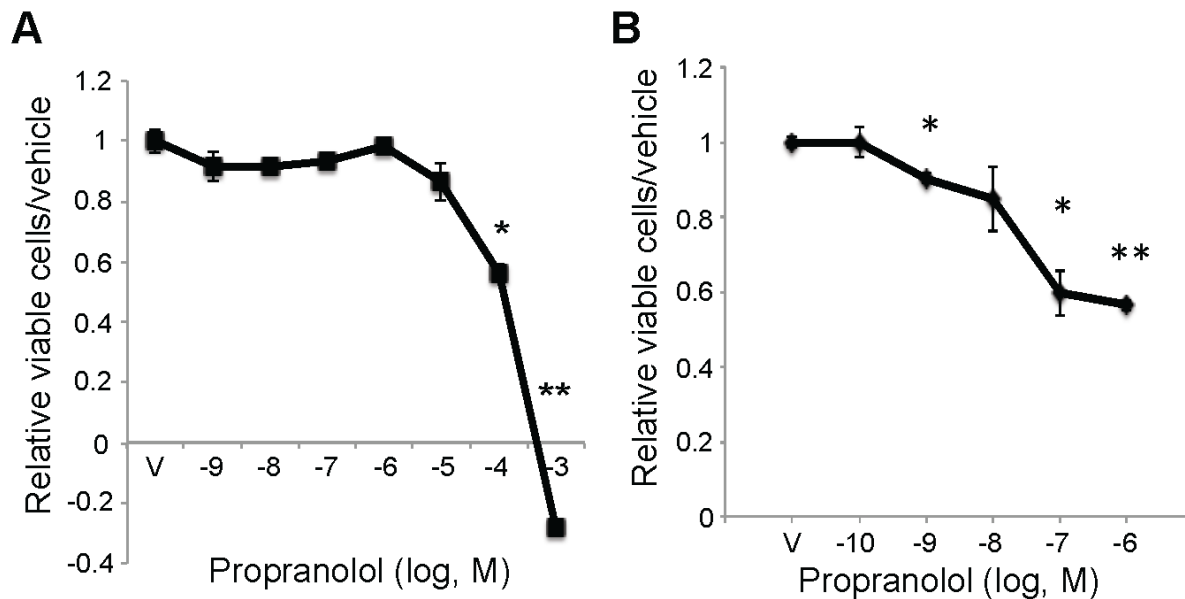


Figure S3. Propranolol suppression of HemSC proliferation and viability increased over time. A)

HemSCs were treated with increasing doses of propranolol over a 7-log dose range (10⁻⁹M to 10⁻³M) and number of viable HemSCs determined at 24 hours. *p<0.002 **p<0.001. **B)** HemSCs were treated with increasing doses of propranolol over a 5-log dose range (10⁻¹⁰M to 10⁻⁶M) and number of viable HemSCs determined at 48 hours. *p<0.02, **p<0.00005 **A,B)** Proliferation presented as fold-difference to vehicle (V) treated HemSCs. Data presented as \pm S.E.M.

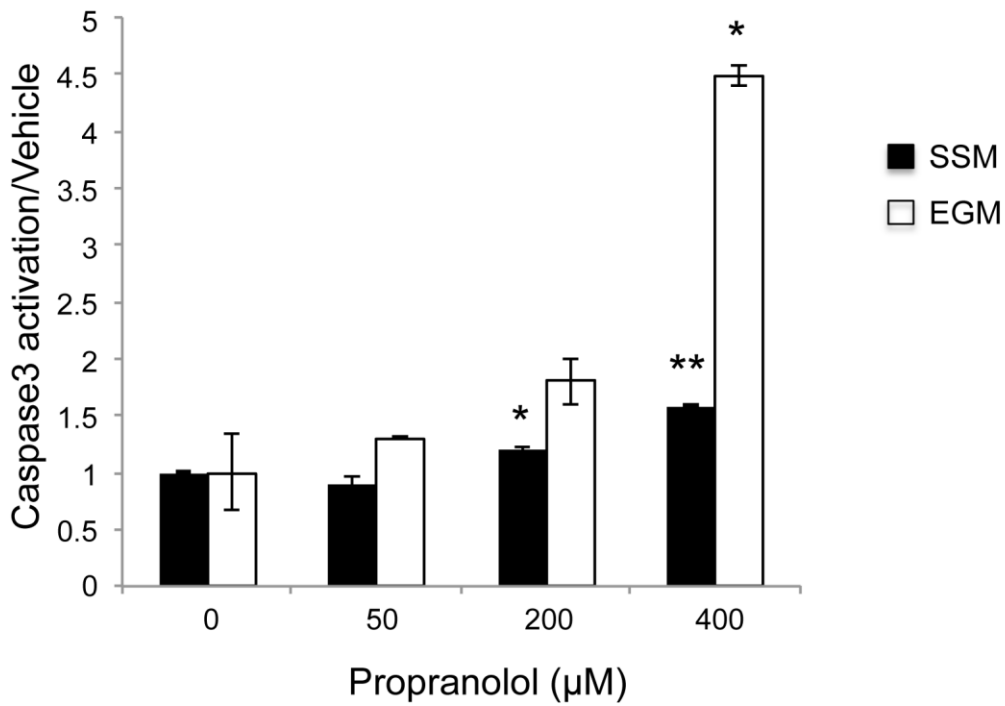


Figure S4. Propranolol activated caspase-3 in HemSCs. HemSCs were treated with 50μM, 200μM, and 400μM propranolol (corresponding to LD₁₀, LD₅₀, LD₉₀) either in the presence or absence of serum and caspase-3 activation assessed at 24hrs. Data presented as fold activation over vehicle (V) ± S.E.M.

*p<0.001, **p<0.0001.

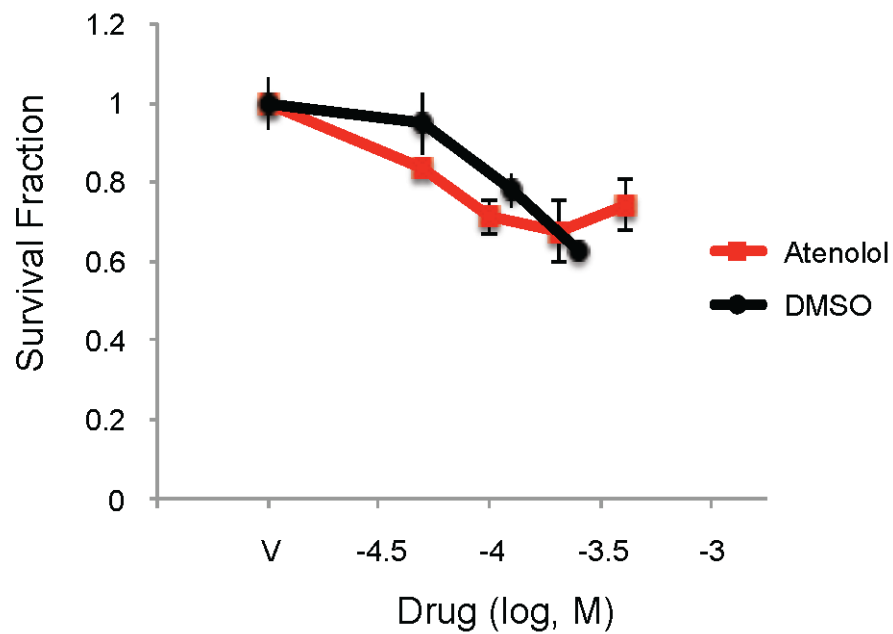


Figure S5. Effects of atenolol on HemSC viability were due to the DMSO diluent. HemSCs were treated with increasing doses of atenolol or equal volumes of DMSO alone and viability assessed by DIMSCAN assay at 24 hours. Data presented as survival fraction of propranolol treated HemSC relative to vehicle (V) controls \pm S.E.M.

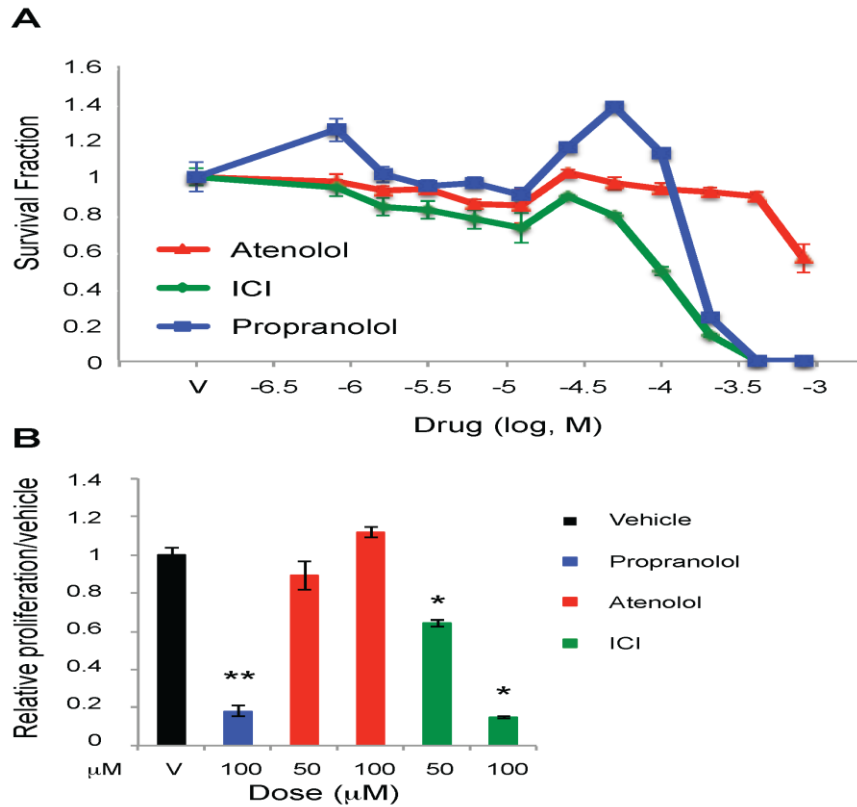


Figure S6. ICI mirrored propranolol effects on MSCs and HemSC behavior. A) Propranolol and ICI treatment dose-dependently suppressed viability and induced cytotoxicity in MSCs. MSCs were treated with increasing doses of atenolol, ICI or propranolol ($10^{-6.5}$ M to 10^{-3} M) and viability assessed by DIMSCAN assay at 24 hours. Data presented as survival fraction relative to vehicle (V) control \pm S.E.M. At doses 200 μ M and higher, viability was significantly greater for cells treated with atenolol when compared to those treated with either ICI, or propranolol. ($p < 0.001$ at 200 μ M, 400 μ M, and $p = 0.002$ at 800 μ M). There was no significant difference in cell viability between cells treated with ICI and propranolol. **B)** ICI suppressed HemSC proliferation similar to propranolol. HemSC were treated with vehicle, propranolol (100 μ M), ICI (50 μ M, 100 μ M), or atenolol (50 μ M, 100 μ M) and number of viable HemSCs determined at 72 hours. Data presented as fold-difference to vehicle (V) treated HemSCs \pm S.E.M. * $p < 0.005$, ** $p < 0.0005$.